The Gamma Knife®

Stereotactic Radiosurgery as an Alternative Surgical Means

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While traditional, invasive neurosurgery has long been the most accepted method of rectifying brain abnormalities, stereotactic radiosurgery is becoming a more frequent, and arguably more efficient approach to treating certain cranial lesions. Despite its name, stereotactic radiosurgery is a non-invasive procedure that does not require opening the skull, which reduces hospitalization time and improves quality of life for patients (Lippitz, 2004). This alternative to conventional surgery focuses multiple high-energy radiation beams on a specific area of the brain in order to irradiate intracranial lesions with minimal destruction of any normal tissue.

The three forms of stereotactic radiosurgery currently in use include the charged Particle Beam (or "Cyclotron"), the Linear Accelerator (commonly referred to as the LINAC system), and the Gamma Knife®. The Particle Beam unit is successful in treating unusually-shaped tumours, as well as those which reside outside of the cranial cavity, such as in the spine and base of the skull (John Hopkins Medicine, 2005). The LINAC system operates by transmitting x-ray photons to destroy cancer cells (Deinsberger & Tidstrand, 2005). The Gamma Knife® is constructed in such a way that numerous, small high-energy gamma ray fields converge on a specific location, making it the most accurate form of stereotaxis. Due to its extraordinary precision, the Gamma Knife® is ideal for targeting small, intracranial tumours that may otherwise be inoperable. This surgical alternative can also be used in conjunction with conventional surgery, allowing for less complicated operations and resulting in fewer risks.

Gamma Knife® surgery can be used to treat many types of brain tumors, whether benign or malignant, primary or metastatic. A primary tumour refers to a growth located at the same site from which it originates, whereas a metastatic tumour develops from cancer cells that have spread from a different location within the body, such as from the breast or lung (Medline Plus Medical Dictionary, 2003). Gamma Knife® surgery is also useful for treating arteriovenous malformations (AVMs), which are among the leading causes of stroke in young people. AVMs are arteries and veins that have tangled and can cause haemorrhage in the brain, as well as headaches and seizures. The Gamma Knife® has proven to be a valuable substitute for invasive surgery, especially in cases where the lesion is embedded deep within the brain, near or inside of vital regions (Kobayashi, Mori & Kida, 2003).

Introduction to Gamma Knife® Surgery

The fundamental principles of stereotactic radiosurgery include the selective irradiation of targeted tissue while sparing the surrounding normal brain tissue and without physically opening the skull. For each Gamma Knife® treatment, ionizing gamma rays are emitted by 201 radioactive cobalt-60 sources with a common focal point, and allows the radiation to converge simultaneously at the target (Papagiannis et al., 2005). The term "gamma ray" refers to the electromagnetic radiation emitted from the nucleus during a radioactive process (Figure 1). Nuclear radiation is a result of the powerful strain between the opposing nuclear strong force and the electromagnetic forces, which are the two strongest basic forces. For this reason, the resulting gamma rays are very high-energy beams of radiation, with wavelengths of less than 1.0×10^{-12} m. With their extremely high energy level, gamma rays possess ionizing properties that can therefore be harnessed for this type of medical treatment (Nave, 2005).

While the radiation does not physically remove the brain abnormality, the emitted photons ionize the targeted tissue mass, triggering the production of free radicals. These inorganic ions are deleterious to the cellular and nuclear membranes of the target cells, as well as to their RNA and DNA molecules. When the procedure is successful, the vital structures of the tumourous cells are destroyed, resulting in cell death and a gradual shrinkage in the volume of tissue until it is completely destroyed. The duration of the process depends on the type of tumour, as it generally requires only a few weeks with regard to metastases, but can take years with slow-growing benign tumours or AVMs. The dose of radiation absorbed by the treated tissue can define the rate of biological inactivation. This is measured in Gray units, where one Gray (Gy) is the absorption of one joule of radiation per kilogram of tissue mass (Guo et al., 2004).

Gamma Knife® Surgery: Procedure

In order to begin treatment with the Gamma Knife®, a local anaesthetic is administered and an aluminium frame is attached to the patient's head, secured with sterile pins. This ensures that there is no head movement throughout the procedure, and that the highly focused gamma rays are appropriately guided to their precise location. With this frame in place, the patient is scanned using computed tomography (CT scan) or magnetic resonance imaging (MRI) technologies in order to determine the exact location of the lesion. The precise coordinates generated from the imaging studies unit are then relayed to the Gamma Knife's® three-dimensional computer planning program. The image from this computer software allows the team of specialized medical professionals to focus the beams on the target area to within 0.3 mm accuracy, decide upon a dose, and calculate the radiation exposure times (Hayashi & Izawa, 2004). Upon completion of this planning, the patient enters the room containing the Gamma Unit, which is composed of a moveable couch and 201 sources of cobalt-60 within a heavy shielded vault. The head frame is secured to a hemispherical helmet with 201 collimator parts that correspond to the radiation sources. To commence treatment, the vault doors open, and the couch advances until the cobalt source and collimators align (Figures 3 and 4). Throughout the treatment, the gamma rays delivered from the helmet's 201 sites converge at the precise coordinates determined during the planning stage. This arrangement ensures that the surrounding tissue receives minimal exposure, while the tumour receives maximum radiation due to the convergence of all of the beams (Dr. A. Kaufmann, 2006, personal communication) (Figure 4). The positive effects of a Gamma Knife® treatment are realized over time. Upon completion of the treatment, periodic imaging studies may be conducted, depending on the target (University of Maryland Medical Centre, 2004).

Gamma Knife® Surgery: Pros and Cons

Although Gamma Knife® surgery is still evolving with regard to its applications, it has been deemed successful at treating a variety of intracranial conditions. This technology was first developed in 1962 in Sweden and became widespread in the 1980s, with units located in a variety of countries. There are currently over 200 Gamma Knife® units worldwide, and over 300 000 patients have been treated (Medical College of Georgia, 2005). Canada did not begin using the Gamma Knife® technology until 2003, when the first unit was installed at the Health Sciences Centre in Winnipeg, Manitoba, making this still a relatively new form of surgical treatment for Canadian patients (WRHA, 2003). Despite its many benefits, Gamma Knife® surgery is associated with inherent risks, such as cerebral edema (swelling of the brain), radionecrosis (the death of brain tissue), and cranial nerve palsy (loss of sensation or movement, due to injury of the cranial nerves) (Medline Plus Medical Dictionary, 2003). Studies have shown that conventional radiation therapy has induced secondary neoplasia in patients, or tumour formation, many years after their treatment is completed (Ganz, 2002). Since gamma radiation ionizes matter, it is also capable of producing adverse physiological effects in cells, including mutations or cancer. Initially, treatment with the Gamma Knife® can put patients with left temporal lobe epilepsy at a higher risk of seizures, but overall, the long-term effect includes a reduction in the occurrence of seizures (Ganz, 2002). There may also be neuropsychological side effects for these patients, as studies indicate some experience a significantly delayed verbal memory for up to two years following treatment with the Gamma Knife®. (McDonald et al., 2004). In most cases, however, the risks associated with Gamma Knife® treatment are lower than those associated with either open surgery or with leaving the disease untreated. While Gamma Knife® surgery can offer therapeutic benefits in certain cases, these advantages must be weighed against the associated disadvantages for each individual patient before determining whether results will be more favourable with this non-invasive procedure or with conventional surgery.

Arteriovenous Malformations

Although 60% to 70% of patients with AVMs are treated with conventional microsurgery, Gamma Knife® treatment has become an accepted alternative for all AVMs smaller than 3.5 cm in diameter. Certain patients are considered unsuitable candidates for invasive surgery, such as in cases where the abnormality lies in vital portions of the brain or is surgically inaccessible (Kobayashi, Mori & Kida, 2003). Studies show, however, that unlike conventional surgery, this form of stereotactic radiosurgery does not protect the patient from the

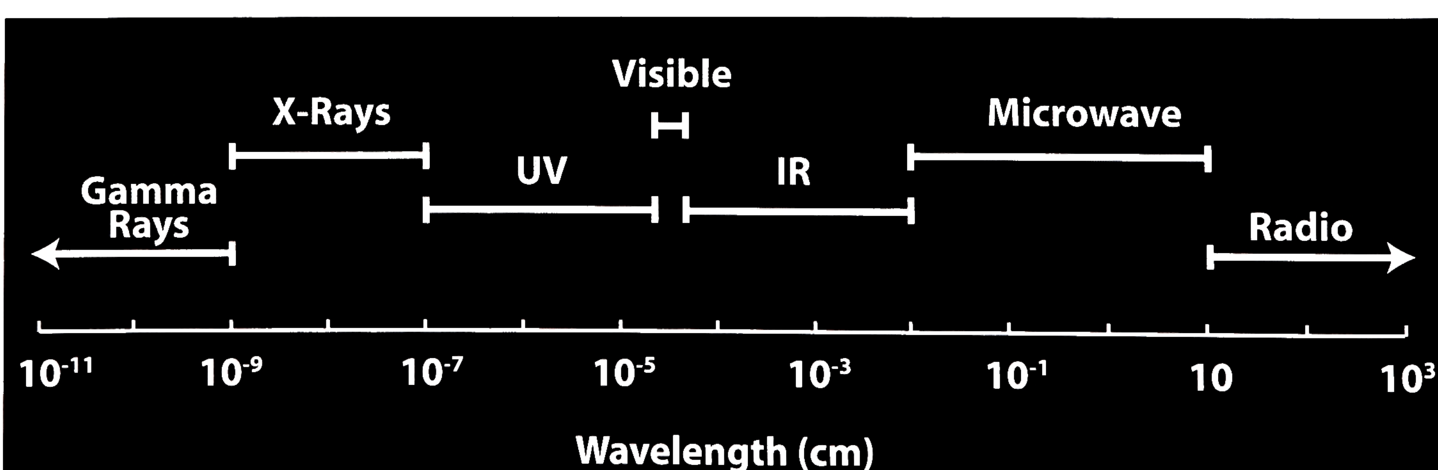

Figure 1: The Electromagnetic Spectrum. Gamma Ray, on the far left of the spectrum range in wavelength from 10^{-9} cm downwards (Nave, C.R., 2005).

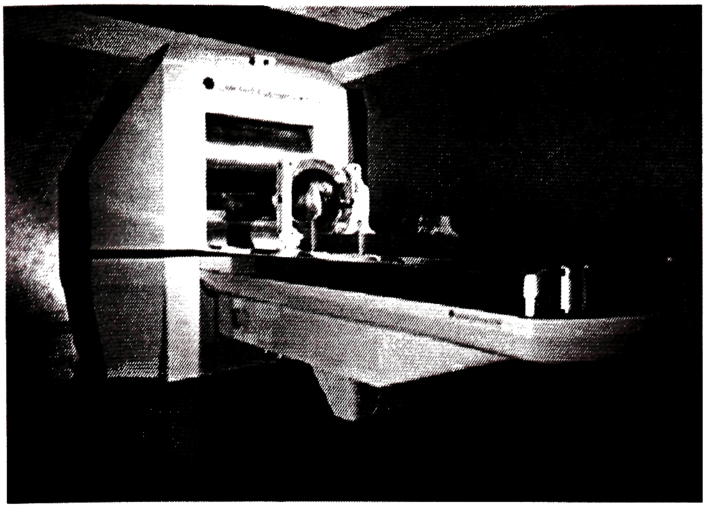

Figure 2: Gamma Knife® Unit, composed of moveable couch and hemispherical helmet containing 201 cobalt-60 radiation sources (Indiana University School of Medicine, 2004).

risk of haemorrhage before the abnormality has been occluded. Despite the fact that complications with Gamma Knife® surgery include bleeding during the latency period after the surgery, the risks associated with traditional neurosurgery are still greater (Kaufmann, 2006, personal communication).

Benign Brain Tumors

In many cases, complete surgical removal is the preferred method of treating benign tumours; however, Gamma Knife® radiation is the treatment of choice in instances where patients are likely to experience surgical complications, or where the tumor is located near a vital location of the brain. Success rates following treatment with the Gamma Knife® of benign tumours are up to 90%, in which there is no further growth over a follow-up period of at least four years. (Minnesota Department of Health, 2004).

Malignant Brain Tumors

Gamma Knife® surgery is highly effective in treating brain metastases 3 cm in diameter or smaller. Studies indicate a very low rate of associated morbidity, as well as very successful rates of local tumour control (Lippitz, 2004). This form of radiosurgery is also valuable in treating multiple metastases, as well as lesions that are resistant to traditional radiation therapy (Lippitz, 2004). Gamma Knife® radiation is especially useful in treating brain metastases due to melanoma and renal cancer. These lesions are particularly radio-resistant and therefore require the high doses which can be delivered with the Gamma Knife® (Tarhini & Agarwala, 2004). There is still controversy, however, as to whether treatment of these lesions with Gamma Knife® surgery increases survival rates in comparison to conventional radiation therapy (Kaufmann, 2006, personal communication). Gamma Knife® surgery is now also used to treat individuals with multiple brain tumours. In one study involving patients with multiple newly diagnosed intracranial metastases from known primary cancer locations (the primary cancer being lung cancer in 66% of the cases), the growth of tumours was arrested in 82% of subjects treated with the Gamma Knife® (Jawahar et al., 2005). All of the patients in the study had 3 or more metastatic brain tumours, and treatment with radiosurgery positively affected survival rates after diagnosis with the brain disease. (Jawahar et al., 2005). In terms of primary malignant brain tumours, the Gamma Knife® is not typically used as a method of treatment as of yet. (Minnesota Department of Health, 2004).

Trigeminal Neuralgia

Trigeminal Neuralgia is a disorder of cranial nerve V (the trigeminal nerve), causing attacks of intense pain on one side of the face where the branches of this nerve are distributed (John Hopkins Medicine, 2005). In recent years, Gamma Knife® radiosurgery has become a widely used treatment for people unresponsive to other medical therapies for trigeminal neuralgia, and is also an alternative to more invasive surgical options. Increased experience with its use, along with advances in imaging, have underscored the importance of the Gamma Knife® as a treatment option (John Hopkins Medicine, 2005). This method of treatment does pose some disadvantages, however, for although it is perhaps the safest and easiest surgical treatment available for Trigeminal Neuralgia, it is also associated with a delay of a few weeks prior to pain relief, as well as with the lowest chances of permanent pain relief (John Hopkins Medicine, 2005).

Gamma Knife® Surgery: Conclusion

The introduction of Gamma Knife® surgery into the Canadian healthcare system has successfully offered hope to patients who are poor candidates for conventional surgery or who prefer a less invasive treatment. Although use of Gamma Knife® surgery has only been implemented within the last few decades, it has been very effective in treating common neurosurgical diseases, and its future remains very positive. A number of future applications are currently being investigated, including treatments for Parkinson's Disease, epilepsy and other neurological disorders (Jawahar et

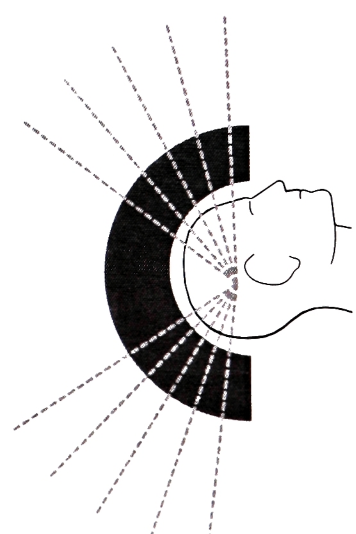

Figure 3: Gamma Knife® approach: beams of gamma radiation are emitted from 201 cobalt-60 radiation sources, so that the surrounding tissue receives minimal exposure, and the rays converge on a precise targeted location. In this way, the area within 0.1 mm accuracy of the coordinates is the only tissue receiving maximum ionization from the radiation (Mayo Clinic, 2004).

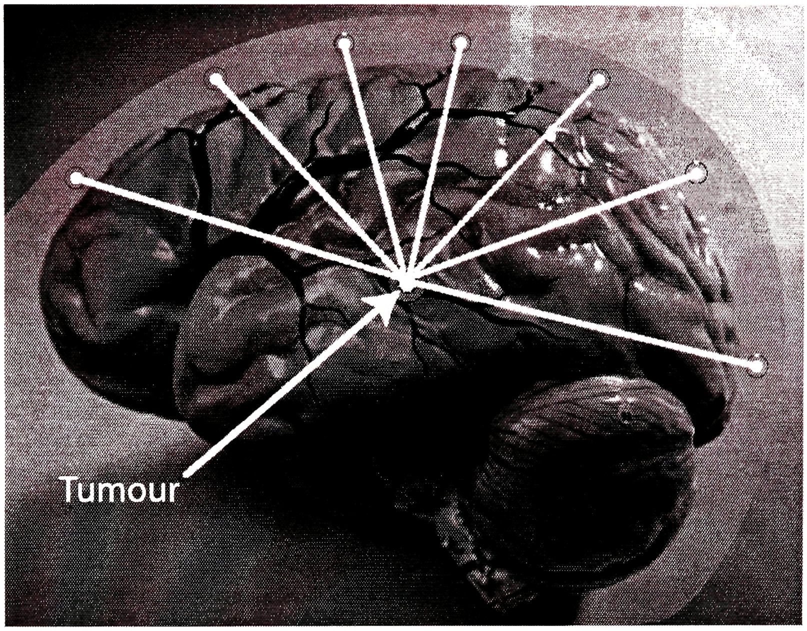

Figure 4: The Gamma Knife® bombards the tumour with multiple beams of gamma radiation (BBC News Online, 1998).

al., 2004). As the Gamma Knife® emerges as a primary method of treatment for many brain disorders, new possibilities for this technology will arise, widening the scope of patient care (Jawahar et al., 2004). Presently, however, the Gamma Knife® improves the quality of life for many patients with brain abnormalities (Hayashi & Izawa, 2004). By shortening hospitalization times, reducing post-operative side effects, eliminating the risks associated with anaesthesia, and removing the need for lengthy radiation therapy following intensive neurosurgery, it is no wonder that the Gamma Knife® is considered by many patients to be a miracle treatment.

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